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ACUTE AND CHRONIC TOXICITY OF
2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN IN MINK

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Two studies were conducted in which adult mink were either exposed acutely or chronically to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). In both studies, all animals were housed singly and given pelleted feed and water ad libitum. Food consumption and body weight changes were determined weekly. During daily observation periods, all signs of intoxication and/or mortality were recorded. All animals were subject to gross necropsy at time of death or at termination of the study. Blood samples were taken from surviving animals immediately preceding termination for analyses of blood parameters and the lymphocyte response to the mitogen concanavalin A (Con A) and pokeweed.

In the first study, 16 adult male mink (four mink per treatment group) were administered single oral doses of TCDD at 0, 2.5, 5.0, and 7.5 $\mu\text{g}/\text{kg}$ body weight and observed for 28 days. All mink administered 7.5 μg died by day 14 while mortalities for the 5 μg group (75%) occurred during the first 17 days. The oral LD_{50} value was determined to be 4.2 μg TCDD/kg body weight. Mink in all treatment groups showed significant ($P < 0.05$) dose-dependent weight loss when compared to controls. However, food consumption was significantly ($P < 0.01$) depressed only in the 5.0 and 7.5 $\mu\text{g}/\text{kg}$ groups. In the 5.0 $\mu\text{g}/\text{kg}$ group, food consumption was comparable to control during the final 14 days of the study.

Gross necropsy revealed discoloration and mottling of the liver, spleen, and kidneys. The only significant alteration of organ weights, expressed as a percent of brain weight, was a significant increase in adrenal weights in the 2.5 and 7.5 μg groups.

Red and white blood cell counts, hematocrits, and hemoglobin concentrations in the surviving mink were not significantly altered. Lymphocyte proliferation response to Con A was not significantly altered by TCDD exposure.

In the second study, 56 adult female mink (eight mink per treatment group) were exposed to 0, 0.001, 0.01, 0.1, 1.0, 10, or 100 ppb TCDD via the diet for a total of 125 days. A 28-day dietary LC_{50} of 4.3 ppb was calculated. The 100 ppb and 10 ppb groups displayed 100% mortality by 28 and 49 days, respectively. The 1.0 ppb group had 63% mortality at the termination of the study at 125 days. Food consumption by the 0.0, 0.001, 0.01, and 0.1 ppb treatment groups was comparable during the entire 125-day study. Food consumption was significantly depressed in the 1.0 ppb group during week 8 ($P < 0.05$), in the 10 ppb group during weeks 4 and 5 ($P < 0.01$), and in the 100 ppb group during weeks 1 and 3 ($P < 0.01$). There was significant loss of body weight in the 10 and 100 ppb groups, with some animals experiencing greater than 50% weight loss by time of death. Based on the mortality for the 18 week study, a 125-day dietary LC_{50} of 0.85 ppb was calculated.

In addition to the characteristic "wasting syndrome", heart weights were significantly ($P < 0.01$) decreased in the 1.0 ppb group and spleen weights were significantly depressed in the 10 and 100 ppb groups. Adrenal weights were significantly ($P < 0.05$) elevated in the 1.0, 10, and 100 ppb groups when compared to controls. Mottling and discoloration of the liver, spleen, and kidneys were observed in all groups exposed to TCDD. Ascites was occasionally observed in the higher treatment groups.

Blood parameters were not significantly altered by TCDD treatment. Lymphocyte proliferation responses in the groups evaluated (control, 0.01, and 0.1 ppb) were not significantly different.

These results indicate that mink are among the most sensitive species to 2,3,7,8-TCDD based on the calculated LD₅₀ and LC₅₀ values. Because of its sensitivity and because it is a carnivore which consumes fish in the wild, the mink can serve as a valuable model to study the impact of environmental polyhalogenated compounds on mammalian species.

TITLES OF MANUSCRIPTS AND DISSERTATIONS

MANUSCRIPT

Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin to mink. J.R. Hochstein, R.J. Aulerich, S.J. Bursian, and A.C. Napolitano. (In preparation).

DISSERTATION

Toxicological manifestations of 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure to mink. J.R. Hochstein, Ph.D. Dissertation. (In preparation).

POSTER


Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in mink. J.R. Hochstein, R.J. Aulerich, S.J. Bursian, and A.C. Napolitano. 6th Annual Meeting, Society of Environmental Toxicology and Chemistry. November 10-13, 1985, St. Louis, MO. (Abstract attached).

NAMES AND TITLES OF PERSONNEL

R.J. Aulerich, Professor
S.J. Bursian, Associate Professor
J.R. Hochstein, Graduate Research Assistant
A.C. Napolitano, Fur Farm Manager
B.A. Olson, Laboratory Technician

DESCRIPTION AND STATUS OF INVENTIONS

None



Steven J. Bursian, Principle Investigator

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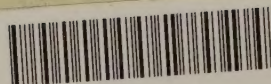
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TOXICITY OF 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN
TO ADULT MINK: J.R. Hochstein, R.J. Aulerich,
S.J. Bursian, A.C. Napolitano, Department of
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Adult female mink (Mustela vison) were fed diets containing 0.00, 0.001, 0.01, 0.1, 1.0, 10.0 or 100.0 ppb 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) for 28 days. In addition, adult male mink were administered oral dosages of 0.00, 0.001, 0.01, 0.1, 1.0 or 10.0 µg TCDD/kg body weight. Food consumption and body weight changes for all animals were determined weekly. Food and water were available ad libitum. Following in-test mortality and upon termination of the studies expired animals were subject to gross necropsy. The Litchfield-Wilcoxon method for evaluating dose-response experiments was used to determine a dietary LC₅₀ of 4.3 ppb TCDD for adult female mink. Results of the range finding test for adult male mink indicate that the LD₅₀ for TCDD would be 1.0 to 10.0 µg/kg body weight. These findings indicate that mink are among the most sensitive species to 2,3,7,8-TCDD.



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